

Claims

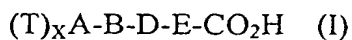
A

Method of using

1. Use of compounds the generalized formula (I):

 $\Lambda$ 

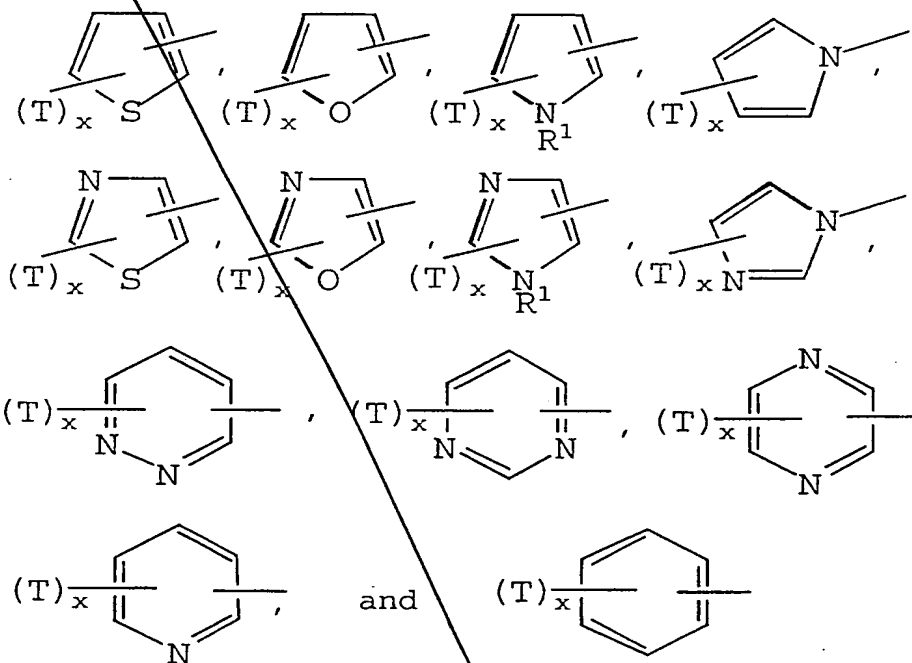
5



wherein

(a)  $(T)_x A$  represents a substituted or unsubstituted aromatic or heteroaromatic moiety selected from the group consisting of:

10



wherein R<sup>1</sup> represents H or alkyl of 1 - 3 carbons; and

15

each T represents a substituent group, independently selected from the group consisting of:

- \* the halogens -F, -Cl, -Br, and -I;
- \* alkyl of 1 - 10 carbons;
- \* haloalkyl of 1 - 10 carbons;
- \* haloalkoxy of 1 - 10 carbons;

20

\* alkenyl of 2 - 10 carbons;

\* alkynyl of 2 - 10 carbons;

~~\*~~  $-(\text{CH}_2)_p\text{Q}$ , wherein

p is 0 or an integer 1 - 4,

\* -alkenyl-Q, wherein

said alkenyl moiety comprises 2 - 4 carbons, and

\* -alkynyl-Q, wherein

said alkynyl moiety comprises 2 - 7 carbons; and

Q is selected from the group consisting of aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, -CN, -CHO, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>2</sup>, -OCOR<sup>2</sup>, -SOR<sup>3</sup>, -SO<sub>2</sub>R<sup>3</sup>, -CON(R<sup>4</sup>)<sub>2</sub>, -SO<sub>2</sub>N(R<sup>4</sup>)<sub>2</sub>, -C(O)R<sup>2</sup>, -N(R<sup>4</sup>)<sub>2</sub>, -N(R<sup>2</sup>)COR<sup>2</sup>, -N(R<sup>2</sup>)CO<sub>2</sub>R<sup>3</sup>, -N(R<sup>2</sup>)CON(R<sup>4</sup>)<sub>2</sub>, -CHN<sub>4</sub>, -OR<sup>4</sup>, and -SR<sup>4</sup>;

wherein

$R^2$  represents H;

alkyl of 1 - 6 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

R<sup>3</sup> represents alkyl of 1 - 4 carbons;

aryl of 6 - 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom; or

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons; or

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

$R^4$  represents H;

alkyl of 1 - 12 carbons;

aryl of 6 -10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl in which the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 4 carbons;

heteroaryl-alkyl in which the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

alkenyl of 2 - 12 carbons;

alkynyl of 2 - 12 carbons;

~~-(C<sub>q</sub>H<sub>2q</sub>O)<sub>r</sub>R<sup>5</sup> wherein q is 1-3; r is 1 - 3; and R<sup>5</sup> is H provided q is greater than 1, or alkyl of 1 - 4 carbons, or phenyl;~~

alkylenethio terminated with H, alkyl of 1-4 Carbons, or phenyl;

alkyleneamino terminated with H, alkyl of 1-4 carbons, or phenyl;

-(CH<sub>2</sub>)<sub>s</sub>X wherein s is 1 - 3 and X is halogen;

$$-\text{C}(\text{O})\text{OR}^2; \text{ or}$$
$$-\text{C}(\text{O})\text{R}^2;$$

and with the provisos that a) when two R<sup>4</sup> groups are situated on a nitrogen, they may be joined by a bond to form a heterocycle, and

b) unsaturation in a moiety which is attached to Q or which is part of Q is separated from any N, O, or S of Q by at least one carbon atom, and

$x$  is 0, 1, or 2;

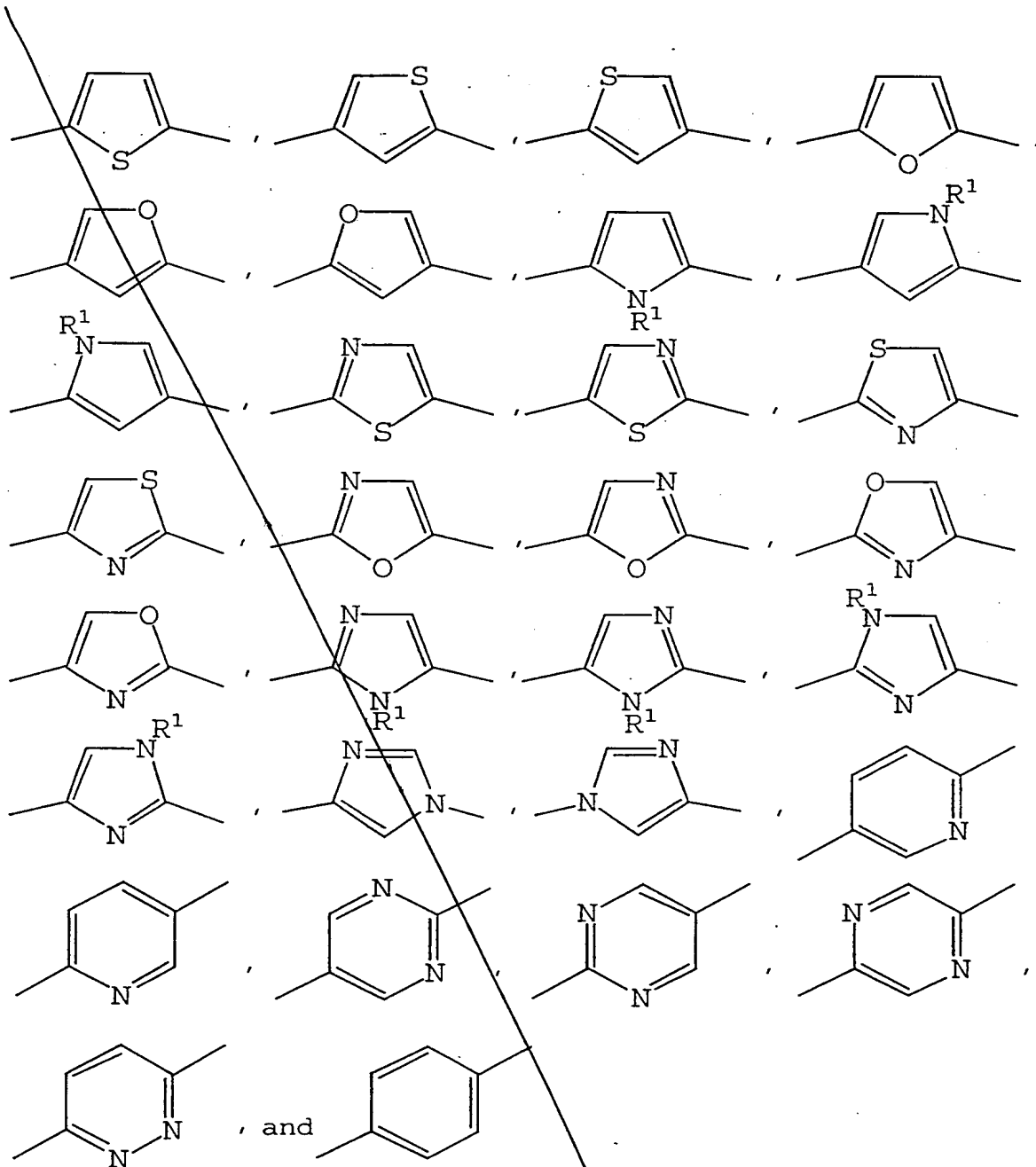
(b) B represents a bond or an optionally substituted aromatic or hetero-aromatic ring containing 0-2 substituents T, which substituents T may independently have the meaning specified under (a), the B rings being selected from the group consisting of:

10

Sub  
B1

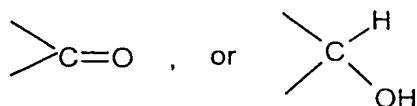
5

[illegible]



5

(c) D represents



(d) E represents a chain of n carbon atoms bearing m substituents  $R^6$ , wherein said  $R^6$  groups are independent substituents, or constitute spiro or nonspiro rings in which a) two groups  $R^6$  are joined, and taken together with the chain atom(s) to which said two  $R^6$  group(s) are attached, and any intervening chain atoms, constitute a 3 - 7 membered ring, or b) one group  $R^6$  is joined to the chain on which said one group  $R^6$  resides, and taken together with the chain atom(s) to which said  $R^6$  group is attached, and any intervening chain atoms, constitutes a 3 - 7 membered ring; and wherein

n is 2 or 3;

m is an integer of 1 - 3;

each group  $R^6$  is independently selected from the group consisting of:

- \* fluorine;
- \* hydroxyl, with the proviso that a single carbon may bear no more than one hydroxyl substituent
- \* alkyl of 1 - 10 carbons;
- \* aryl of 6 - 10 carbons;
- \* heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;
- \* arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;

\* heteroaryl-alkyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 8 carbons;

\* alkenyl of 2 - 10 carbons;

\* aryl-alkenyl wherein the aryl portion contains 6 - 10 carbons and the alkenyl portion contains 2 - 5 carbons;

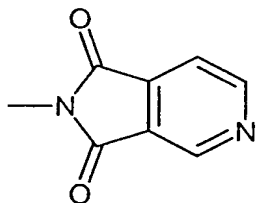
\* heteroaryl-alkenyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkenyl portion contains 2 - 5 carbons;

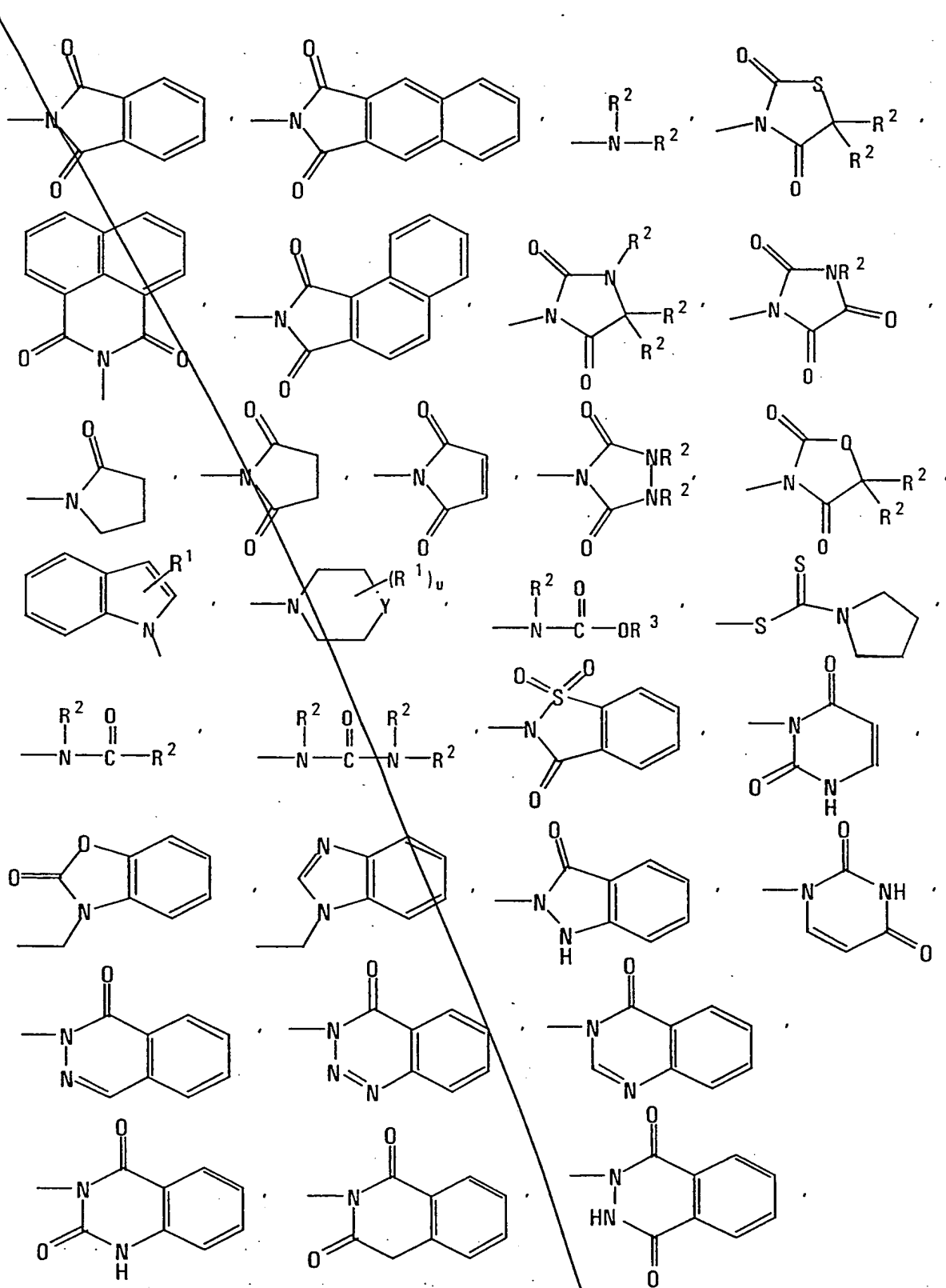
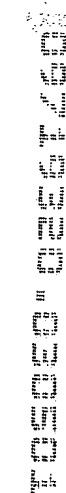
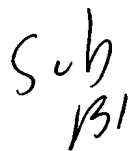
\* alkynyl of 2 - 10 carbons;

\* aryl-alkynyl wherein the aryl portion contains 6 - 10 carbons and the alkynyl portion contains 2 - 5 carbons;

\* heteroaryl-alkynyl wherein the heteroaryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkynyl portion contains 2 - 5 carbons;

\*  $-(CH_2)_t R^7$  wherein  
t is 0 or an integer of 1 - 5; and  
 $R^7$  is selected from the group consisting of







and corresponding heteroaryl moieties in which the aryl portion of an aryl-containing R<sup>7</sup> group comprises 4 - 9 carbons and at least one N, O, or S heteroatom;

wherein

Y represents O or S;

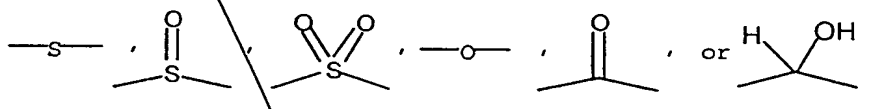
~~R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> are as defined above and each R<sup>1</sup>, R<sup>2</sup> or R<sup>3</sup> may be the same or different; and~~

$u$  is 0, 1, or 2; and

\*  $-(\text{CH}_2)_v\text{ZR}^8$  wherein

$v$  is 0 or an integer of 1 to 4; and

Z represents



$R^8$  is selected from the group consisting of:

alkyl of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion contains 6 to 10 carbons and the alkyl portion contains 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion comprises 4 - 9 carbons and at least one N, O, or S heteroatom and the alkyl portion contains 1 - 4 carbons;

-C(O)R<sup>9</sup> wherein R<sup>9</sup> represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion contains 6 - 10 carbons or is heteroaryl comprising 4 - 9

carbons and at least one N, O, or S heteroatom, and the alkyl portion contains 1 - 4 carbons;

and with the provisos that

- when  $R^8$  is  $-C(O)R^9$ , Z is S or O;

- when Z is O,  $R^8$  may also be  $-(C_qH_{2q}O)_rR^5$  wherein q, r, and  $R^5$  are as defined above; and

\*  $-(CH_2)_wSiR^{10}_3$  wherein

w is an integer of 1 to 3; and

$R^{10}$  represents alkyl of 1 to 2 carbons;

and with the proviso that

- aryl or heteroaryl portions of any of said T or  $R^6$  groups optionally may bear up to two substituents selected from the group consisting of  $-(CH_2)_yC(R^4)(R^3)OH$ ,  $-(CH_2)_yOR^4$ ,  $-(CH_2)_ySR^4$ ,  $-(CH_2)_yS(O)R^4$ ,  $-(CH_2)_yS(O)_2R^4$ ,  $-(CH_2)_ySO_2N(R^4)_2$ ,  $-(CH_2)_yN(R^4)_2$ ,  $-(CH_2)_yN(R^4)COR^3$ ,  $-OC(R^4)_2O-$  in which both oxygen atoms are connected to the aryl ring,  $-(CH_2)_yCOR^4$ ,  $-(CH_2)_yCON(R^4)_2$ ,  $-(CH_2)_yCO_2R^4$ ,  $-(CH_2)_yOCOR^4$ , -halogen, -CHO,  $-CF_3$ ,  $-NO_2$ , -CN, and  $-R^3$ , wherein

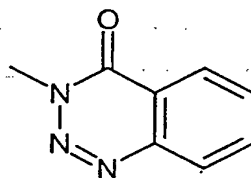
y is 0 - 4; and

$R^3$  and  $R^4$  are defined as above, and each  $R^3$  or  $R^4$  may be the same or different; and any two  $R^4$  which are attached to one nitrogen may be joined to form a heterocycle;

and pharmaceutically acceptable salts and prodrugs thereof ~~for the manufacturing of drugs~~ for the treatment and prevention of cerebral diseases.

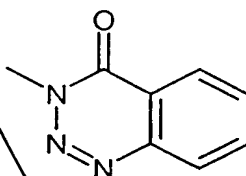
### Method of using

2. Use of compounds of the generalized formula (I) according to claim 1, wherein  $R^6$  is  $-(CH_2)_tR^7$ , in which t is 0 or an integer 1-5, and  $R^7$  is a group of the formula



*A* and pharmaceutically acceptable salts and prodrugs thereof ~~for the manufacturing of drugs~~ for the treatment of cerebral diseases.

- 5 *A* 3. *Method of using*  
~~Use of~~ compounds of the general formula (I) according to claim 1, wherein E represents a chain of 2 carbon atoms bearing 1 substituent  $R^6$ , and wherein  $R^6$  is  $-(CH_2)_tR^7$ , in which t is 0 or an integer 1-5, and in which  $R^7$  is a group of the formula



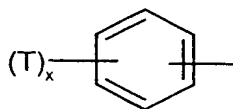
10

*A* and pharmaceutically acceptable salts and prodrugs thereof ~~for the manufacturing of drugs~~ for the treatment of cerebral diseases.

15

4. *Method of using*  
~~Use of~~ compounds of the generalized formula (I) according to claim 1, wherein

(a)  $(T)_x A$  represents a the group of the formula



20

wherein

T represents a substituent group, independently selected from the group consisting of:

- \* the halogens -F, -Cl, -Br, and -I;
- \* alkyl of 1 - 10 carbons;
- \*  $-(CH_2)_pQ$ , wherein  
p is 0 or an integer 1 - 4, and

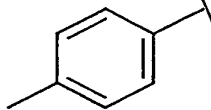
Q is  $-OR^4$ ,

wherein

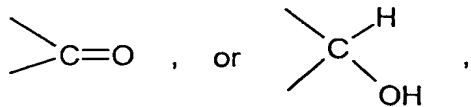
$R^4$  represents alkyl of 1 - 12 carbons;

x is 0, 1, or 2;

(b) B represents a group of the formula:



(c) D represents



(e) E represents a group of the formula  $-CH_2-CHR^6-$ ,

wherein

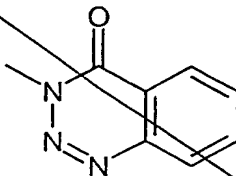
$R^6$  is a group of the formula  $-(CH_2)_tR^7$ ,

wherein

t is 0 or an integer of 1 - 5; and

Sub  
B1

R<sup>7</sup> is a group of the formula



- 5 and with the proviso that the aryl portion of said R<sup>6</sup> group optionally may bear up to two substituents selected from the group consisting of -halogen, -CHO, -CF<sub>3</sub>, -NO<sub>2</sub>, and -CN,

- 10 A and pharmaceutically acceptable salts and prodrugs thereof ~~for the manufacturing of drugs~~ for the treatment and prevention of cerebral diseases.

- A 5. *Method according to claim 2*  
~~Use according to any of claims 2 to 4,~~ wherein the compound of the general formula (I) is an alkali metal salt or an alkaline earth metal salt.

- 15 A 6. *Method according to claim 2*  
~~Use according to any of claims 2 to 5,~~ wherein the compound of the general formula (I) is a sodium salt.

- A 7. *Method according to claim 2*  
~~Use according to any of claims 2 to 6,~~ wherein the application is parenteral.

- 20 A 8. *Method according to claim 2*  
~~Use according to any of claims 2 to 6,~~ wherein the application is intravenous.

- A 9. Alkali metal salt or alkaline earth metal salt of a compound of the general formula (I) according to <sup>claim 2</sup>~~any of claims 2 to 4.~~

- 25 10. 4-(4'-Chloro-biphenyl-4-yl)-4-oxo-4H-benzo[d][1,2,3]triazin-3-yl)ethyl]-butyric acid sodium.

- 
11. Pharmaceutical composition ~~A~~ comprising at least one compound according to claim 9 or 10.
- 

add  
A2